Peritoneal Dialysis International, Vol. 34, pp. 289–298
doi: 10.3747/pdi.2012.00248

0896-8608/14 $3.00 + .00
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OUTCOMES OF PERITONEAL DIALYSIS PATIENTS AND SWITCHING TO HEMODIALYSIS: A COMPETING RISKS ANALYSIS

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♦ ***Background:*** **We performed a review of a large incident peritoneal dialysis cohort to establish the impact of current practice and that of switching to hemodialysis.**

♦ ***Methods:*** **Patients starting peritoneal dialysis between 2004 and 2010 were included and clinical data at start of dialysis recorded. Competing risk analysis and Cox proportional hazards model with time-varying covariate (technique failure) were used.**

♦ ***Results:*** **Of 286 patients (median age 57 years) followed for a median of 24.2 months, 76 were transplanted and 102 died. Outcome probabilities at 3 and 5 years respectively were 0.69 and 0.53 for patient survival (or transplantation) and 0.33 and 0.42 for technique failure. Peritonitis caused technique failure in 42%, but ultrafiltration failure accounted only for 6.3%. Davies comorbidity grade, creatinine and obesity (but not residual renal function or age) predicted technique failure. Due to peritonitis deaths, technique failure was an independent predictor of death hazard. When successful switch to hemodialysis (surviving more than 60 days after technique failure) and its timing were analyzed, no adverse impact on survival in adjusted analysis was found. However, hemodialysis via central venous line was associated with an elevated death hazard as compared to staying on peritoneal dialysis, or hemodialysis through a fistula (adjusted analysis hazard ratio 1.97 (1.02 – 3.80)).**

♦ ***Conclusions:*** **Once the patients survive the first 60 days after technique failure, the switch to hemodialysis does not adversely affect patient outcomes. The nature of vascular access has a significant impact on outcome after peritoneal dialysis failure.**

Perit Dial Int **2014; 34(3):289–298 www.PDIConnect.com**
epub ahead of print: 04 Feb 2014 doi:10.3747/pdi.2012.00248

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Received 22 September 2012; accepted 15 April 2013.

KEY WORDS: Epidemiology; technique failure; survival; body mass index; vascular access.

Peritoneal dialysis (PD) as a mode of renal replacement therapy has witnessed divergent trends in the last decade. While the outcomes continued to improve and were comparable to hemodialysis (HD) (1), the proportion of end-stage renal disease patients treated with this modality in developed countries declined (2). During this time, many investigative efforts of the PD community have been focused on studying the impact of new, more biocompatible solutions which became available around the start of millennium (3–5). The possible benefits of the novel solutions included preservation of peritoneal membrane function and a lower incidence of ultrafiltration failure (3,6), less systemic inflammation (7), preservation of residual renal function (8,9) and improved patient survival (10,11). However, most of these benefits were shown in non-randomized studies which were not supported by other studies and some of the benefits may have other explanations unrelated to biocompatibility (12). Perhaps even more important to PD therapy in the last decade has been a growing utilization of icodextrin and automated peritoneal dialysis (APD) (13–15). Although modifications to fluids and practices in PD have the potential to improve outcomes, large randomized controlled trials are lacking. It is also possible that a more restrictive patient selection during this period influenced the observed outcomes (1) and therefore continuing to monitor PD outcomes is a necessity.

While multicenter and registry cohort studies have the advantage of large patient numbers which allow comparisons between dialysis modalities, single center studies can provide a more detailed description of patient outcomes and causes of technique failure. In a landmark

report comprehensively describing the outcomes of a PD cohort between 1990 and 1998 (16), the main causes of technique failure were peritonitis and ultrafiltration failure. Technique failure was associated with poorer survival and fast solute transport predicted technique failure and death. Sudden death and debilitation were the most common modes of death. Although in the following decade several reports have described patient outcomes (17,18), for a proper insight into the evolution of PD therapy and comparison to previous data there is a need to have the most recent data on PD outcomes preferably from a similar population and socioeconomic background. Furthermore, as there is concern about the potentially fatal complications of long-term PD therapy, the impact of switching to hemodialysis and the timing of this switch become more important to the long-term management of PD patients. There is however, a paucity of outcome data for PD patients after a switch to HD when compared to staying on PD (19,20) and available data are contradictory.

This study was designed to investigate the long-term association of technique failure with patient survival and the importance of the timing of this event. The hazard of dying of patients who had switched to HD was compared to those who are still on PD. We investigated whether this hazard depends on the type of HD access. To properly investigate these issues we also gathered information on the association of other variables with technique and patient survival, causes of technique failure and modes of death.

SUBJECTS AND METHODS

STUDY DESIGN

The study was designed as an observational retrospective single-center cohort study. All patients who were intended to start with peritoneal dialysis at our center in the time period between 01.01.2004 and 31.12.2010 as a mode of chronic renal replacement therapy were considered for inclusion in the study cohort. They were not included if the following conditions were present: (i) PD training period not being successful and patients converted to HD due to mechanical catheter problems; (ii) duration of HD before PD start more than 120 days; (iii) quick renal recovery eliminating the need for further dialysis treatment; (iv) short PD trial then decided to stop dialyzing and (v) transfer out of the center or lost to follow up immediately after PD start. The study cohort was therefore limited to patients successfully established on PD beyond the training period and treated with PD as their first mode of renal replacement therapy, with a pre-specified short period of preceding HD allowed. The PD training period on average lasted 5 days. The date of the start of PD training was used as an entry time point for survival analyses.

BASELINE COVARIATES

Patient and hospital records were used for data gathering including the results of diagnostic studies. Patient clinical characteristics and routine laboratory results at the first clinical visit after start of PD treatment were used as baseline covariates. Patient comorbidity at this time point was assessed by the Davies comorbidity score (21). Peritoneal adequacy assessment and peritoneal equilibration test (PET) were made using the PD Adequest software package according to the manufacturer's guidelines (Baxter Healthcare Corporation, McGraw Park, Illinois, USA). These assessments yielded the values of residual glomerular filtration rate, calculated as a mean of renal creatinine and urea clearance and total weekly urea Kt/V. First adequacy assessment and PET after PD start were used as baseline covariates. Patients were designated as treated with APD when this modality was used for the majority of time spent on PD.

Outcomes: Each subject was followed until death, transplantation or until 01.03.2011 when all observations were stopped (censored). Patients who transferred out to other centers were designated as lost to follow-up and censored in survival analyses. The date and cause of PD technique failure were noted for all cases. Death due to peritonitis was defined as any death during treatment of a peritonitis episode or hospitalization for peritonitis. Death due to peritonitis was taken as one of the causes of technique failure. Such patients were designated as treated only with PD, disregarding any short pre-terminal period of HD treatment, if present. Interim periods of HD treatment due to leaks or other transient complications were disregarded if the patient subsequently continued with PD regardless of the length of this period. After the switch to HD, the predominant type of vascular access for a particular patient was defined (arteriovenous (AV) fistula or graft and central venous line). If the patient had successful AV fistula established as vascular access any time after the switch, he was regarded as an AV fistula patient, if not, he was regarded as central venous line patient. The modes of death were defined using a previously published approach (16) and divided into the following categories: sudden out of hospital death and/or cardiovascular event, debilitation with or without dialysis withdrawal, peritonitis, other infectious diseases (i.e., non peritoneal sepsis), malignancy, mixed (when

several diseases were contributing to death as sequential complications), other and unidentified causes.

STATISTICAL METHODS

Characteristics of the study cohort are described using medians and ranges for the continuous variables and proportions for the categorical variables. The differences between the groups were calculated using Mann-Whitney and chi-square test, respectively. Since the transplanted patients are not a random sample from the cohort, death, transplant and, additionally, technique failure are regarded as competing events in our analyses. This is particularly relevant when analyzing the probabilities – censoring the transplanted patients and using the Kaplan-Meier estimator would incur a bias and cumulative probabilities of finishing in a certain state are estimated instead (the analysis of competing risks).

When analyzing the association of covariates with the hazard of the event of interest, the Cox model is used, treating all other competing events as censored: the hazard of technique failure is analyzed regarding transplants and deaths as censoring and the analysis of the association of switching to HD and mortality hazard is performed with transplants regarded as censoring. This analysis was repeated twice: first using the actual dates of technique failure, thus determining if technique failure is an adverse event, and secondly moving the times of HD start forward for 60 days, thus regarding deaths within two months from the switch as associated with PD and comparing the hazard of being on one of both modalities studied (on PD or on HD after successful switch from PD).

Since all patients start on PD, treatment modality (HD or PD) was regarded as a time-varying variable in all the analyses. Schoenfeld residuals were used to check whether the hazard ratio of the two modalities changes with time since PD start and to check whether peritonitis as a cause of technique failure has a long-term impact on the hazard of the patients who have switched to HD. Unadjusted and adjusted survival analyses were performed on the same sample size (patients with missing values in adjusted analysis were excluded from unadjusted analysis to ensure a more direct comparison).

The review was approved and registered as an audit with the hospital trust's Audit Committee. The analyses were done using the IBM SPSS and R statistical packages.

RESULTS

Between 1.1.2004 and 31.12.2010, 309 patients who were starting with PD at our center were eligible to be included in the study. Of these, 23 patients were excluded due to above pre-specified exclusion criteria (Figure 1). The remaining 286 patients represent the study cohort. Of these, 155 were active on the renal transplant waiting list and 76 (26.8%) were transplanted during the follow-up period, 104 (36.2%) were alive at 01/03/2011, 102 (35.6%) died and 4 (1.4%) were lost to follow-up. The cohort was followed up until death or transplantation or until lost from follow-up. The median follow-up time was 24.2 months (range 0.8 – 84.2 months).

PATIENT CHARACTERISTICS

The characteristics of the study cohort are shown in Table 1. Data are described for the whole study cohort and for the two subgroups – 'PD maintained' and 'PD technique failure'. The PD maintained subgroup of 191 patients includes all patients who remained on PD until the end of the study on 01/03/2011 or were transplanted or died while on PD (all causes of death except peritonitis). The PD technique failure group comprises 95 patients with technique failure who were switched from PD to HD including patients who died because of peritonitis (n = 13). Patients with technique failure

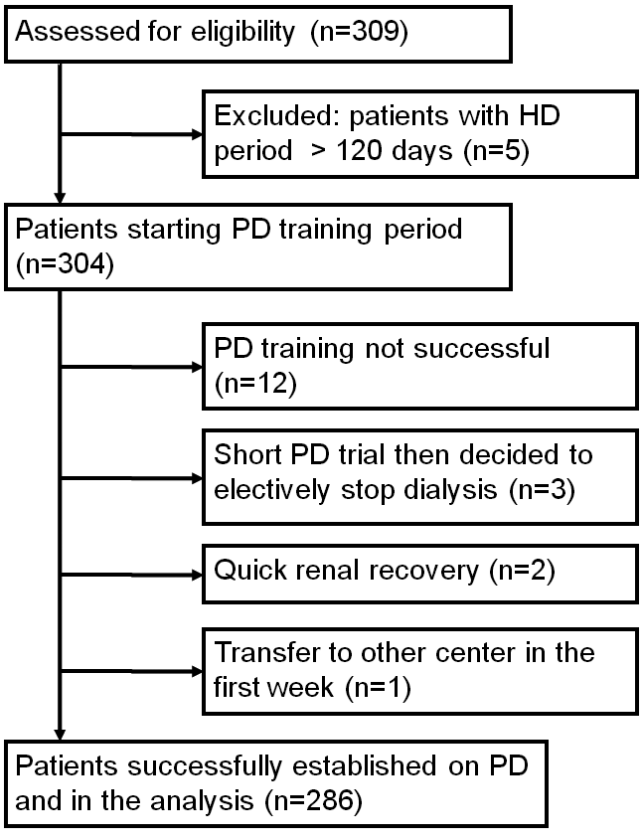

Figure 1 — The consort diagram of patient selection for analysis. HD = hemodialysis; PD = peritoneal dialysis.

TABLE 1
Clinical Characteristics of the Study Cohort

Parameter	All (*n*=286)	PD maintained (*n*=191)	PD failure (*n*=95)	$p^{\dagger}$
Age	56.5 (17.3–5.8)	53.6 (17.6–85.8)	60 (17.3–84.3)	0.26
Gender				
Female (%)/male (%)	112 (39%)/174 (61%)	76 (40%)/115 (60%)	36 (38%)/59 (62%)	0.76
Davies comorbidity grade				
Grade 0, *n* (%)	114 (40%)	84 (44%)	30 (32%)	0.13
Grade 1, *n* (%)	137 (48%)	86 (45%)	51 (54%)	
Grade 2, *n* (%)	35 (12%)	21 (11%)	14 (14%)	
DM present	94 (33%)	59 (31%)	35 (37%)	0.31
Previous CV event	63 (22%)	38 (20%)	25 (26%)	0.22
Transplant list activated	154 (54%)	109 (57%)	45 (47%)	0.12
APD/CAPD	194 (68%) / 92 (32%)	131 (69%)/ 60 (31%)	63 (66%)/ 32 (34%)	0.7
BMI, *n*=247	25.5 (17–43.9)	25.2 (17–40.6)	27 (17.9–43.9)	0.02
Total weekly Kt/V, *n*=247	2.21 (0.79–5.19)	2.26 (1.07–5.19)	2.07 (0.79–4.2)	0.016
GFR (mL/min/1.73m^2), *n*=247	4.8 (0–16.1)	5.3 (0–16.1)	4.4 (0–14.37)	0.001
Daily diuresis (mL), *n*=266	1080 (0–4040)	1260 (0–4040)	935 (0–2770)	0.002
Total fluid removal (mL/day), *n*=247	1810 (290–5030)	1810 (290–4210)	1830 (490–5030)	0.73
PET 4h D/P creatinine, *n*=180	0.71 (0.44–0.98)	0.68 (0.44–0.98)	0.75 (0.47–0.98)	0.09
Albumin (g/L)	37 (20–49)	38 (20–49)	37 (21–49)	0.13
Creatinine (µmol/L)	603 (186–1712)	597 (186–1376)	624 (252–1712)	0.11
Hemoglobin (g/L)	118 (78–169)	118 (78–169)	118 (78–164)	0.82

PD = peritoneal dialysis; DM = diabetes mellitus; CV = cardiovascular; APD = automated peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; BMI = body mass index; GFR = residual glomerular filtration rate; PET = peritoneal equilibration test; D/P = dialysate to plasma ratio. The data in parentheses for continuous variables is range and for patient numbers the percent within group (column).
† Mann-Whitney and chi-square test for continuous and categorical variables, respectively.

had higher body mass index (BMI) and lower residual renal function; otherwise the groups were comparable. Diabetic kidney disease was the most prevalent cause of renal failure (27%), followed by interstitial, cystic and hereditary diseases (20%), primary glomerulopathies (17%), multisystem diseases (including atherosclerotic, hypertensive, autoimmune and paraproteinemic – 15%) and unknown causes (21%).

COMPETING RISK ANALYSIS OF TECHNIQUE AND PATIENT SURVIVAL

The estimated probabilities of experiencing one of the competing risks (death and transplantation) for the PD cohort are shown in Table 2. In addition, the probabilities of technique failure (as a competing risk with death and transplantation) were calculated and added to Table 2.

Three- and five-year probabilities of survival on dialysis (or being transplanted) were 0.69 and 0.53 for patient survival and 0.33 and 0.42 for technique failure (Table 2). Median time on dialysis (time to transplant or death) was 2.73 years (95% CI [2.41, 3.21]), median time on PD (time to technique failure, transplant or death) was 1.80 years (95% CI [1.59, 2.21]). It is notable that the risk of technique failure in the small number of long-term PD survivors after the 4th year on PD rises only very slowly.

PD TECHNIQUE FAILURE – CAUSES AND PREDICTIVE FACTORS

Technique failure occurred in 95 patients, and the causes are shown in Table 3. Peritonitis was the single most common cause of technique failure, followed by failures due to choice or not coping and leaks or mechanical problems. Pure ultrafiltration failure as a cause of PD failure was present in 6.3% of patients.

The significant factors affecting technique failure hazard in univariate regression were BMI (borderline), serum creatinine, residual GFR and unplanned start of renal replacement therapy (start with HD and switching to PD). In the multivariate Cox proportional hazard model, only Davies comorbidity, serum creatinine and BMI remained significant independent predictors of technique failure (Table 4). Peritoneal transport rate as measured by dialysate to plasma ratio of creatinine at 4-hour PET did

TABLE 2
Cumulative Probabilities of Transplantation, Death and Technique Failure

Time (years)	Number of patients at risk	Probability of transplantation	Probability of death	Probability of technique failure
1	211	0.09	0.09	0.1
2	141	0.16	0.19	0.24
3	87	0.23	0.31	0.33
4	50	0.30	0.37	0.37
5	25	0.32	0.47	0.42
6	13	0.36	0.50	0.42
7	1	0.36	0.52	0.43

Numerical values of cumulative probabilities of transplantation and death in the PD cohort. In the last column the cumulative probability of technique failure is shown, regarding transplantation and death as competing events for technique failure.

TABLE 3
Causes of PD Technique Failure and Modes of Death in the Study Cohort

PD technique failure cause	Number of patients (%)	Mode of death	Number of patients (%)
Peritonitis	40 (42%)	Sudden death / cardiovascular event	32 (31.4%)
Choice or not coping	15 (15.8%)	Debilitation with(out) dialysis withdrawal	19 (18.6%)
Leak or mechanical problems	14 (14.7%)	Peritonitis	13 (12.7%)
Inadequate solute removal	10 (10.5%)	Infections	10 (9.8%)
Ultrafiltration failure	6 (6.3%)	Malignancy	7 (6.9%)
EPS or EPS suspicion	4 (4.2%)	Mixed	6 (5.9%)
Other	6 (6.3%)	Other	2 (2.0%)
		Not known	13 (12.7%)

PD = peritoneal dialysis; EPS = encapsulating peritoneal sclerosis. Total number of patients – 286, total number of technique failures – 95, total number of deaths – 102.

TABLE 4
Predictors of Technique Failure

Covariate	Unadjusted HR (95% confidence interval)	Adjusted HR (95% confidence interval)	*p* (adjusted)
Age (years)	1 (0.99–1.01)	1.01 (0.99–1.02)	0.53
Female Gender	0.78 (0.49–1.23)	1.27 (0.69–2.32)	0.45
Davies comorbidity grade 1	1.54 (0.94–2.54)	**2.2 (1.23–3.92)**	**0.008**
Davies comorbidity grade 2	2.01 (0.98–4.13)	**3.19 (1.34–7.6)**	**0.009**
GFR (mL/min/1.73m^2)	**0.88 (0.81–0.95)**	0.97 (0.87–1.08)	0.55
Serum creatinine (μmol/L)	**1.002 (1.001–1.003)**	**1.003 (1.001–1.004)**	**0.001**
Serum albumin (g/L)	0.97 (0.92–1.02)	0.97 (0.92–1.03)	0.36
BMI (kg/m^2)	**1.04 (1–1.09)**	**1.06 (1.01–1.11)**	**0.018**
APD (vs CAPD)	0.85 (0.52–1.39)	0.72 (0.43–1.21)	0.21
HD start	**1.94 (1.06–3.56)**	1.73 (0.87–3.45)	0.12

HR = hazard ratio; GFR = residual glomerular filtration rate; APD = automated peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; BMI = body mass index; HD start = having a short period of HD (up to 120 days) before starting with PD. Overall adjusted Cox proportional hazard model: likelihood ratio test=39.9 at 9 degrees of freedom, $p<0.001$. No. of cases with missing values: 39, No. of patients in the analysis: 247, No. of events: 78. Included patients and number of events were the same for unadjusted analysis. The statistically significant results are in bold.

not significantly predict technique survival in univariate or multivariate analysis. However, the number of missing values for this variable was high and the 95% confidence interval was wide. When D/P creatinine ratio was included in the multivariate technique survival model, the HR was 0.61 (0.04 – 9.03), so potentially important effects might have been missed in our sample.

MODES OF DEATH, PREDICTIVE FACTORS OF PATIENT MORTALITY AND THE IMPACT OF SWITCH TO HEMODIALYSIS

Modes of death for the patient cohort are shown in Table 3. Sudden and unexpected out-of-hospital deaths and cardiovascular events were the single most common mode of death, present in 31% of patients. Peritonitis was an important mode of death – present in 13% of patients. For 13 patients, data about cause and mode of death were missing.

The analysis of predictive factors for patient death was focused on the impact of technique failure and the subsequent switch to hemodialysis on mortality hazard and on the comparison of the mortality hazard between the patients who had or had not yet had the switch. For this purpose, the switch to hemodialysis was taken as a time-varying covariate. Besides well-known possible confounders of survival hazard (age, sex, serum albumin, residual GFR), the analyses were adjusted also for factors possibly confounding the association between technique survival and patient survival (comorbidity, BMI and serum creatinine). First, the effect of having PD technique failure was adjusted for the above-mentioned covariates, and it remained a significant predictor of death with HR 3.72 (95% CI 2.26 – 6.13, $p < 0.01$). When deaths in the first 60 days after technique failure were ascribed to PD period and the hazard ratio of the modality adjusted for other covariates, the dialysis modality (PD compared to HD) was no longer an independent predictor of death (HR 1.44, 95% CI 0.83 – 2.49, $p = 0.2$). In the latter analysis 17 deaths were present in the 60-day buffer period and most of them (13 deaths) were due to peritonitis.

The estimated value of the HR for modality proves to be rather constant up to four years after PD start (the curve in Figure 2 presents the log of HR in time), indicating that the exact timing of switch within this period is not affecting mortality. On the basis of our data, this cannot be claimed after this period when confidence intervals get wide (p value for the hypothesis of no change in time is 0.09) and highly negative values indicating patients still on PD having a higher hazard are possible.

Finally, the effect of having switched to HD was analyzed according to the HD vascular access – Table 5. Here, switching to HD with a central venous line as a dialysis

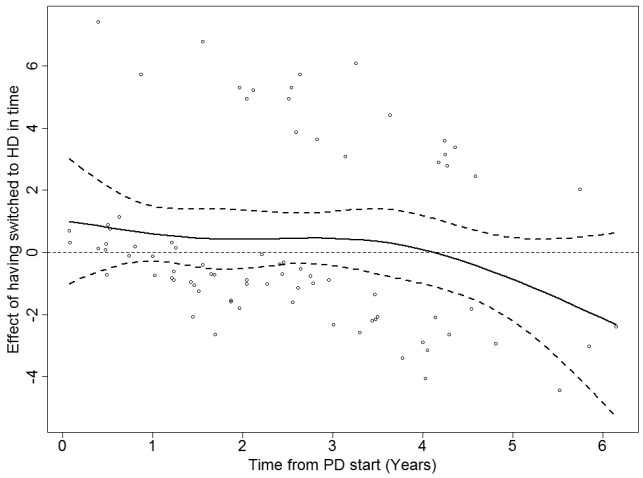

Figure 2 — The course of adjusted log hazard ratio for death (HR of treatment with HD compared to staying on PD in time). Time in x-axis is measured from the PD start. The p value for the change of adjusted log hazard ratio with time is 0.09. HR = hazard ratio; HD = hemodialysis; PD = peritoneal dialysis.

access was associated with a significantly elevated hazard for death compared to reference group (patients staying on PD) adjusted for age, sex, comorbidity, albumin, BMI, creatinine and residual GFR. The hazard of HD through arteriovenous fistula was not significantly different from the reference group.

To better clarify the differences observed in the two analyses with and without the 60-day buffer period, we studied the impact of having switched due to peritonitis. Figure 3 presents the change of log HR (patients who switched due to peritonitis compared to those with other reasons for switching) in time, where time is measured from the switch. Only patients with technique failure are included in this analysis. The change in time is highly statistically significant ($p = 0.001$). It can be seen that while peritonitis patients have a highly elevated hazard shortly after the switch in the first 30 days, later no long-term disadvantage of having switched due to peritonitis can be claimed.

DISCUSSION

In this analysis of a contemporary peritoneal dialysis cohort we present the recent outcomes of PD patients treated at a single center with special emphasis on the outcomes when switching from PD to HD. Although not directly comparable due to methodological differences, the crude three- and five-year survival probabilities of 0.69 and 0.53 are similar to available national registry data from the UK (22), USA (23), Australia (24) and Canada (25). Although survival data for PD cohorts are best evaluated from registry studies, there is a lack of

TABLE 5
Predictors of Patient Death Using Switch to Hemodialysis as a Time-Dependent Covariate

Covariate	Unadjusted HR (95% CI)	Adjusted HR (95%)	*p* (adjusted)
Switch to HD with CVL	**1.95 (1.04–3.66)**	**1.97 (1.02–3.80)**	**0.04**
Switch to HD with fistula/graft	0.69 (0.32–1.47)	0.82 (0.36–1.87)	0.63
Age	**1.06 (1.04–1.08)**	**1.06 (1.04–1.08)**	**<0.01**
Female Gender	0.66 (0.42–1.04)	**0.55 (0.31–0.98)**	**0.04**
Davies comorbidity grade 1	**2.82 (1.53–5.22)**	**2.02 (1.06–3.86)**	**0.03**
Davies comorbidity grade 2	**5.66 (2.81–11.39)**	**3.81 (1.73–8.37)**	**<0.01**
Serum albumin	**0.92 (0.88–0.97)**	0.98 (0.92–1.04)	0.45
Serum creatinine	**0.998 (0.997–1)**	0.999 (0.997–1.001)	0.33
BMI	0.98 (0.94–1.02)	0.98 (0.94–1.03)	0.5
Residual GFR	0.97 (0.90–1.04)	**0.90 (0.81–1)**	**0.04**

HR = hazard ratio; HD = hemodialysis; CVL = central venous line; BMI = body mass index; GFR = glomerular filtration rate. Cox proportional hazard model with time-dependent covariate of switch to HD; likelihood ratio test = 79.6, 10 degrees of freedom, $p<0.001$, number of events = 80. Included patients and number of events were the same for unadjusted and adjusted analysis. 60-day buffer period after PD failure is used. The statistically significant results are in bold.

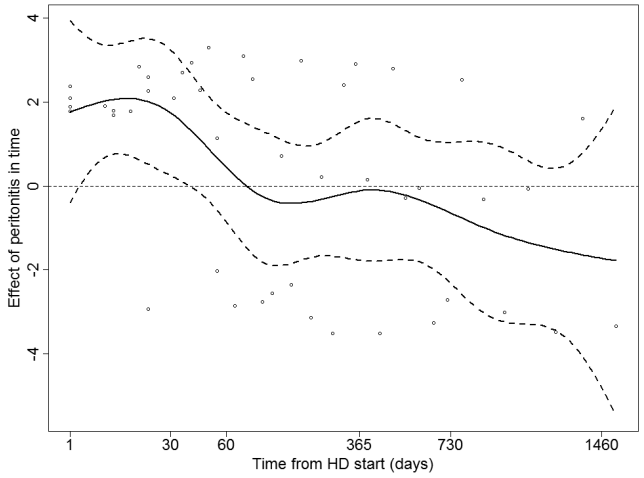

Figure 3 — The course of log hazard ratio for death of peritonitis cases versus others in time. Time in x-axis is measured from the switch to HD. Only patients with technique failure are included. The change in time is highly statistically significant (p=0.001). HD = hemodialysis.

information on comparative outcomes of patients after PD technique failure and the impact of timing of this event. This issue is growing in importance due to the increasing awareness about the complications of long-term PD, such as encapsulating peritoneal sclerosis. In the present analysis we employed the switch to HD as a time-varying covariate in the Cox's proportional hazard model. We have found that technique failure significantly contributes to the hazard of dying and that most of this risk is due to fatal peritonitis cases. After adjustment for the immediate detrimental influence of technique failure *per se* (using the 60-day buffer period) we found that mortality hazard was not significantly different between patients who have successfully switched to HD and those staying on PD (even though they are still at risk of PD-related complications).

When the time course of adjusted hazard of switching to HD was analyzed (Figure 2) it is also clear that, up to four years after PD start there is no difference in adjusted hazard between those staying on PD and those successfully switched to HD (surviving more than 60 days after the switch). After the first four years, the hazard of patients still on PD is getting higher in our sample, but no firm claims can be made due to the drop in the number of patients at risk, and the confidence interval for adjusted hazard widens, not reaching statistical significance.

In general, the trend of improving prognosis if being treated with HD later, after the first years of PD, was reported in the NECOSAD 2 study (26). In that report there was a lower mortality risk for HD-treated patients but only compared to PD patients after two years of PD treatment. On the other hand the most recent report comparing outcomes of PD and HD patients found no differences in survival on both modalities for the cohorts starting dialysis in the 2002 – 2004 period, even late after dialysis start (1). Both these studies included incident patients starting on PD or HD modality, so residual confounding in the factors affecting modality choice may have influenced the results. However, our cohort comprises only patients who started dialysis on PD, and therefore is homogenous in this regard. Our results are similar to the results of Jaar *et al.* (20), showing no difference in survival hazard for patients staying on PD compared to patients with successful switch to HD.

Clearly, to firmly identify the late time point beyond which the transfer to hemodialysis may be definitely protective to patients, we need a study of a much larger PD cohort since there is a large loss of patient numbers beyond four years of PD therapy.

When the outcome of patients after modality switch adjusted for the hemodialysis access type was examined, we found significantly higher mortality hazard for those dialyzing through central venous access as compared to staying on PD. The impact of the hemodialysis access type on the comparative outcomes of HD and PD patients is being increasingly recognized, showing that patients dialyzing through central venous lines have worse survival than PD-treated patients (27). Our results confirm and extend this finding, showing significantly elevated hazard for central venous line-treated patients after PD technique failure in the more homogenous subgroup of PD-first treated patients. Similar results were found for comparison of mortality risk between PD-first and HD-first treated patients (28). However, the comparative outcome of PD patients after technique failure and patients staying on PD with reference to access type has not been reported so far. Full adjustment for the differences between patients who had an arteriovenous fistula and others is difficult to achieve. For example, since patients with an unplanned switch to HD (i.e., peritonitis) are put on i.v. lines first, there may be some confounding on the hazard of lines by the detrimental unplanned causes of switch to HD and this is a limitation of our study. However, there are also well-known detrimental influences of central venous lines *per se*, which have the potential to elevate the mortality hazard (i.e., chronic inflammation at the entry site, higher risk for line sepsis). This observation opens an important area for improving care of PD patients as the dialysis access after PD failure and residual GFR were the only two potentially modifiable predictors of mortality in our analysis (see Table 5).

Peritonitis was the single most important cause of technique failure (42%) and the third ranked cause of mortality (13%) in our cohort. Furthermore, peritonitis-associated deaths were prevailing in the early 60-day period after technique failure (13 out of 17 deaths), thereby causing most of the mortality risk in the early period after technique failure. Additional analysis has shown that having peritonitis as a cause of technique failure had a negative impact on survival only in the immediate 30-day period, but not later on (Figure 3). Although the peritonitis rate was acceptable by current standards for the study period at our center (range of 36 to 20 patient-months per episode), it is interesting to observe that in comparison to the report on causes of technique failure from a decade ago (16), peritonitis in our and other cohorts (29,30) still largely prevails as a cause of technique failure. In contrast, the impact of ultrafiltration failure was much less, and represents only 6% of causes of technique failure in our cohort. This is similar to an Australian report, where ultrafiltration failure represented only 4% of cases (24). Additionally, as a contrast to the report of a 1997 – 2007 PD cohort (31), age was no longer a significant predictor of technique failure, perhaps due to increased utilization of assisted PD in our center. Of the other modifiable factors affecting technique survival we have found a significant impact of obesity, as BMI significantly predicted an elevated hazard of technique failure in adjusted analysis. The elevated risk of higher BMI at start of PD treatment was also reported in other cohorts (20,32) possibly due to higher peritonitis (33) and leak risk (34). Obesity may be a modifiable factor in end-stage kidney disease patients and our results lend further support to efforts of weight control even before the introduction of renal replacement therapy.

Our study has the usual drawbacks of observational cohort studies – such as the inability to control fully for residual confounding beyond covariates taken in adjusted analyses. When adjusting the impact of the technique failure on patient survival, we tried to include all confounders which were associated with technique failure and have the potential to affect patient survival (residual renal function, body mass index, comorbidities, serum creatinine value). Also, the single center nature of the data limits the external validity of the findings. However, as mentioned above, when looking at crude survival this was not substantially different than most recent registry data and the causes of renal failure, technique failure and death are also comparable. More specific to our study is the relatively high number of missing data on residual glomerular filtration rate and peritoneal membrane characteristics (we were only able to obtain PET results for 180 patients). This precludes a more detailed insight into the influence of peritoneal transport on patient outcomes and, although we could show no impact of membrane transport rate on the technique failure rate or patient survival, the important effects of this covariate cannot be fully excluded. Strengths of our study include the use of the competing risks approach, which yields a less biased presentation of survival probabilities than the Kaplan-Meier approach (avoiding the bias caused by censoring the transplanted patients, which are the better prognosis subgroup). Incorporating the time-varying variable of PD to HD switch also enabled us to eliminate the immortal bias on modality comparison.

CONCLUSION

In conclusion, this analysis of a contemporary incident PD patient cohort found a similar mortality hazard for patients switching modality compared to patients staying on PD, but only when the early detrimental effects of technique failure (mostly peritonitis) were accounted for. This observation, however, appears to be limited to patients treated with arteriovenous fistulas and grafts, since patients having central venous lines as dialysis access experienced worse outcomes than patients staying on PD. Regarding the timing of the switch from PD to HD, no significant impact of this timing was found. Peritonitis remains the leading cause of technique failure and an important cause of death as in older reports, but the importance of ultrafiltration failure appears to have diminished. In addition to peritonitis prevention, reduction of weight in obese patients may be tested as one of the potentially modifiable factors that could improve PD technique survival in the future.

DISCLOSURES

Jernej Pajek was supported for this work by grants from Baxter Healthcare, Boehringer Ingelheim (BI) and the Slovenian Research Agency (No. P3-0323). Alastair Hutchison has received research grants and honoraria from Baxter Healthcare. Anand Vardhan has received honoraria from Baxter, BI and Shire.

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